

## Episode 97: This Virus Isn't Done with Us

**Chris Dall:** [00:00:06] Hello and welcome to the Osterholm Update COVID-19, a podcast on the COVID-19 pandemic with Dr. Michael Osterholm. Dr. Osterholm is an internationally recognized medical detective and director of the Center for Infectious Disease Research and Policy, or CIDRAP at the University of Minnesota. In this podcast, Dr. Osterholm will draw on more than 45 years of experience investigating infectious disease outbreaks to provide straight talk on the COVID-19 pandemic. I'm Chris Dall, reporter for CIDRAP News. And I'm your host for these conversations. Welcome back, everyone, to another episode of the Osterholm Update podcast. Over the two years that we've been producing this podcast, there have been some weeks where writing this introduction is more difficult than others. What do you say when things haven't changed all that much from the previous week? That's where I found myself this week. The COVID trends we've been discussing over the previous episodes from the Omicron surge in Asia to the rise of BA.2 in Europe and the declining cases here in the United States all remain. We're just waiting to see what happens next. That being said, there has been some news this week. The FDA has approved a fourth dose of the Pfizer-Biontech and Moderna COVID-19 vaccines and stopped the deployment of a monoclonal antibody in parts of the country where BA.2 is on the rise. And in China, officials appear to be doubling down on their zero COVID policy. We'll discuss all those issues here today in this March 31st episode of the podcast as we assess the state of the COVID-19 pandemic here in the US and around the world. We'll also answer a COVID query about why Africa does not appear to have been hit as hard by the coronavirus as many had feared and share the latest beautiful place submission from one of our listeners. But before we get started, as always, we'll begin with Dr. Osterholm's opening comments and dedication.

**Michael Osterholm:** [00:01:56] Thanks, Chris. It's great to be back with all of you today. For those who are first time listeners, I hope that we're able to provide you with the kind of information that you will find helpful for those who are routine listeners, the podcast family, thank you so much for joining us again. I think there are many of us that are looking forward to the day when these podcasts are no longer necessary or at least relevant, and you can spend your time doing something else that will be much more productive and enjoyable. In the meantime, as you noted in the introduction, Chris, there's a lot going on yet this virus is not done with us. I think that some of the days

ahead are still going to be very challenging in many parts of the world. So we will continue to try to share that kind of information with you that I hope will allow you to understand what's happening, maybe even why it's happening, and most of all, what you can do about it. The dedication today really comes from this experience that we've had since the very beginning of the pandemic and also what it's meant to us personally here at CIDRAP and the podcast team. You know, I can't explain to you in words how much the communications that you have shared with us have meant to us. There have been many, many acts of incredible kindness, thoughtfulness that have made all the difference in the world relative to some of those notes that we get that are threatening, vile and frankly, very, very, very troublesome. We read every piece of mail and email that you send to us, and I wish we could respond back to all of you, just for the sheer sake of time we can't. But today I want to dedicate this podcast to all the kind people who are part of what I call this podcast family. Now, I know that some of you who are listening are going to say, there goes that goofy Mike again, talking about that podcast family and you think it's kind of crazy and you just want me to stick with the science and stick with the data and leave all this other fuzzy stuff out. Well, I can't and I won't. And I'm sorry. I hope that you can forgive me for that, because this is part of the experience. This is part of the pandemic. And I just wanted to acknowledge to each and every one of you listening to this today that you matter, your voice matters, your feedback matters, your kindness matters. And it really is important to us. And so today your goofy podcast guy is dedicating this to you. And specifically I want to note Virginia from Houston, who sent the most lovely, lovely email this week that frankly brought tears to this old Irishman's eyes for the thoughtfulness and the kindness that she expressed to us as a podcast family and specifically to the podcast team. So this podcast is dedicated to all of you who have been so kind and sharing your thoughts, your feelings, your concerns, but all done in the spirit of family. So to you, this podcast is for you. Now in that light, I'm also very happy part of that goofy podcast guy thing to share with you the ever increasing light situation here in Minnesota. Today, March 31st here in Minneapolis, Saint Paul, we will have 12 hours, 44 minutes and 13 seconds of sunlight. Now, I have to admit, that comes off of several days of very cold temperatures with snow. So it's welcome to have that sun. We've gained actually 21 minutes and 59 seconds of sunlight since last week's episode. We are now well past what I would call the tipping point of December 21st, the winter solstice. We've gained 3 hours and 58 minutes and 1 second, almost 4 hours of sunlight since December. So celebrate that. That is a good thing. Enjoy it. And for all of you in the southern hemisphere, as I say, weekly, we're

channeling this light back to you. And so now we're going to move on and hopefully get to for those of you who want that hardcore science, that information you're looking for, but to the rest of you who want that and the ability to feel part of something very special, welcome on board.

**Chris Dall:** [00:06:20] So Mike, let's start with the news out of China, where officials in Shanghai earlier this week initiated a staggered lockdown that closed non-essential businesses, halted public transportation and confined much of their population to their homes. This was in response to what has been the largest outbreak in China since the pandemic began. Mike, you've talked a lot about how China is going to deal with the Omicron variant. Can they pull this off?

**Michael Osterholm:** [00:06:45] Well, Chris, I know I'm going to sound a lot like a broken record here, but let me just start out by saying that what's happening in China right now was inevitable and with Omicron should not have been unexpected. As you know, back in January 28th, I wrote an op ed piece in The New York Times, along with Zeke Emanuel, talking about China's zero-COVID policy in the age of Omicron was doomed to fail. And while it didn't happen immediately and some thought, ha, ha, there you go again, scariness. It did happen eventually. And that's where they're at right now. So let me let me provide some context to this and why this is such an important issue in understanding where they're at. At first blush, many of you say, well, heck, there aren't that many cases in China compared to the rest of the world. And look at the population they have. Why is this a problem? Well, first of all, let me be really clear that it's all about one very specific aspect of this virus. Until Omicron, the infectiousness of the previous SARS-CoV-2 variants was such that they could stop it much like a forest fire. Yeah, it burned. Yeah, it took off. Yeah, it caused damage, but it was brought to an end. Omicron goes from the forest fire analogy to that of the wind. You can't stop the wind. You can deflect it, you can try to divert it, but you can't stop it. And that's the difference in infectiousness between these viruses. The kinds of measures that they took over the course of the past two years were successful with less infectious viruses. So this is a very important point. The second thing is, is that in China, a zero-COVID policy means even one case is a crisis. Even one case results in an extensive response unlike anything we see anywhere else in the world. They shut down over several cases, entire communities in ways that we would have only done had we had many hundreds and hundreds and hundreds of cases in that same community. And so these are the two

elements that make up the ingredients that are so important to understanding what's happened in China. So let's just be really clear right now. Prior to Omicron, I think China had a lot to say as to when and how this virus would be transmitted in their communities by doing these extensive lockdowns, bringing it under control. Yes, it had its flaws, that approach. And it was not easy. Some would say draconian, but their zero-COVID playbook did what the country wanted to do, stamping out transmission of the virus over a relatively short period of time in any one province or city. However, with Omicron, they have now entered this whole new ball game, and it's like Minnesota weather in terms of trying to understand what the conditions are in China. If you don't like the weather today in Minnesota, just wait one day and you'll get something very different. And what's happening right now with Omicron, it's like that. It's a whole new weather game with them. Now, Zeke and I shared in our New York Times op ed, China needed to recognize that this variant was going to be the challenge to their very strategy, and that because it was so much more infectious and because they weren't going to stop it, the methods that they had touted as being so successful over the course of the last two years were doomed to fail. We also laid out in that op ed that there are other issues of the country are dealing with, including their vulnerability to their health care systems, which really lacks the capacity to deal with the sudden surge of patients. Also, they relied on domestic vaccines that just didn't work as well against the variant as did our vaccines here in the United States, or, for that matter, in much of the free world. In other words, China had to prepare for the possibility that their zero-covid playbook might not be enough. And they did not. As I mentioned a moment ago, even a few cases with a zero-COVID policy can result in major lockdowns. Right now, Chris, the Chinese are currently facing their largest outbreak because of Omicron since the very start of the pandemic, with more than 70,000 total cases detected across all 31 of the country's provinces. On Tuesday, they reported nearly 7,000 cases nationwide, more than half of which come from the city of Shanghai. Of course, it was announced this past weekend that Shanghai, which is home to 26 million residents, would be locking down for mass testing efforts, with officials planning to test residents from the eastern half of the city this week and the western half after that. According to reports, city residents can only leave their homes for testing, even walking outside whether it's just to take out the trash or take the dog for a quick walk isn't allowed. A story published in New York Times on Tuesday added more context to this situation. In which they described for some, the restrictions are now life threatening. A number of residents haven't had access to critical treatments, like even dialysis. In one situation, a nurse experienced an asthma attack

ended up dying after being turned away from the hospital that was reportedly closed for COVID disinfection. In addition, businesses and factories are facing the reality of either quickly adapting their approach or shutting down. For example, earlier this week, it was announced that a Tesla factory would be temporarily closed due to the city's restrictions. Otherwise, some factories have continued operation by reducing personnel and even setting up a closed loop system where workers literally sleep, live and work at their place of employment. So you can see that the officials there are willing to go just about any lengths to try and maintain their zero-COVID approach. And for context, this is happening in a city larger than 48 of our 50 states. Think of that. Shanghai, by itself as a city, is larger than 48 of our 50 states. But what happens in the near term if these measures don't work? What if Shanghai is still seeing cases a week from now or two weeks from now or even a month? Remember in northeastern China, there is an entire province home to 24 million residents that has been locked down since mid-March. Still, even two weeks later, they're still reporting increasing cases. Meanwhile, there's also been numerous reports of food shortages in several other cities there. So overall, I don't see how any way China will completely extinguish these different flare ups. Obviously, they're going to great lengths to do that, and it's worked for them in part. But Omicron is so different. Finally, even in the event that these outbreaks are somehow controlled, it might be a matter of days or weeks before the virus pops up in another part of the country, and this process starts all over again. In other words, I really don't think this approach is realistic or sustainable, which is what I said in that January New York Times piece. Similar sentiments this week are being offered in publications by a number of editorial boards, including the Financial Times, The Guardian and The Washington Post. So at this point, Chris, I think China has to acknowledge that reality and make every effort possible to shore up vulnerabilities. Of course, one huge challenge they have there is the lack of vaccination in their older populations. According to an analysis by the Financial Times, more than 130 million residents in China that are at least 60 years of age or older have yet to receive three doses of vaccine. For context, if those 130 million residents somehow form their own country, it would be the 10th most populous in the world. Think of that. These are highly vulnerable people in China making up what would be the 10th most populous population in the world. Recent studies have shown that with Sinopharm and Sinovac, which are the inactivated vaccines that China has largely relied on, three doses are absolutely essential when it comes to preventing severe disease and death. In fact, the latest study from Hong Kong showed that Sinovac's effectiveness against death in older individuals went from 50%

with just one dose to 77% following two doses, and it did achieve 98% after three doses. For how long that protection lasts, we don't know. Note that just 20% and I want to repeat that 20% of Chinese residents 80 years or older have had three doses. At this point, more than 40% of that same age group lacks a single dose, a single dose. Finally, if that's not already enough, many of these older individuals lacking the protection from vaccine live in rural parts of the country where there aren't a lot of hospitals or doctors. So in short, the situation in China isn't great. And while you can't change the past, I think China really could have placed themselves in a much better position if they had just acknowledged early on that the threat that Omicron posed to their Zero-COVID approach and made every effort to vaccinate its population, particularly the oldest residents with three doses. Of course, they've announced recent efforts like mobile vaccination clinics to help do that. But the clock is really ticking. Overall, I don't see any quick or easy solutions for China. And whether the rest of the world wants to admit it or not, China's problem is our problem. Clearly, there's the issue of supply chains which were already being challenged. What would additional delays mean for things like life saving drugs that come out of China or other key resources and commodities that we rely on? There are so many that we do depend upon for our critical supply chains. Let me just add one additional piece to the international picture. While COVID activity has been dropping for weeks or even months in many parts of Africa, the Americas, Southeast Asia and the Eastern Mediterranean, I think the impact of this virus is going to be felt for quite some time. The virus is not done with us, even though many of us are done with the virus.

**Chris Dall:** [00:16:55] In Europe, BA.2 seems to still be driving cases upward in countries like France, but cases in Germany and several other European countries appear to be plateauing or even heading back downward. So Mike, is the BA.2 wave starting to turn in Europe?

**Michael Osterholm:** [00:17:12] Chris, last week we discussed the rise in cases in Italy, the UK, France, Ireland, Belgium, Austria, Switzerland and Germany. This week, five of those countries Italy, the UK, France, Ireland and Belgium are still seeing case numbers rise, with France having the greatest increase at 94%. Three of the countries Austria, Switzerland and Germany are beginning to see cases decline, with Germany seeing the largest drop at 51% over the last two weeks. It's unclear why cases have fallen in some countries while they continue to rise in others. Again, the statement of humility. We don't

necessarily know what's happening here. The prevalence of BA.2 continues to grow both in countries that are seeing increases in cases and those that are seeing decreases. And the variant became dominant at around the same time in both groups of these countries. It also does not appear to be related to the timing of the surge, as most of these countries saw their cases begin to increase in the first few days of March. Again, regardless of whether they are seeing an increase or decrease now. The only possible change that might help explain what happened in Austria is that they reinstated its FFP2 respirator mandate. Again, the kind of respirators similar to our N95s. They mandated that in all indoor spaces such respirators must be used. But still, this could at best explain what's going on only in Austria, still leaving the situation in Switzerland and Germany unclear. And even then there could still be other factors contributing to Austria's decline in cases that we don't understand. The burden of severe disease and deaths from the surge continues to be lower than what Western Europe had experienced in previous surges, despite the fact that many of the countries that I mentioned earlier are seeing increases in new hospitalizations and numbers of patients in the ICU. In last week's podcast, I compared the current number of ICU patients, hospitalizations and deaths to the numbers we saw during the 2020-2021 winter surge in four Western European countries Italy, the U.K., France and Germany. This week, I want to provide some additional context to these numbers. Though the relatively low numbers of ICU patients, hospital admissions and deaths are promising in and of themselves, this is especially reassuring as daily cases now are far higher than they were during the previous surges. Again, we are seeing far more cases now than we were then, but the number of ICU patients, new hospital admissions and deaths are still lower. In short, think of this as an emerging pandemic, where what the impact of a certain number of cases might have been two years ago from a standpoint of need for hospitalization, the occurrence of severe illness and deaths is different now with this more infectious virus, yet one that is not causing the same level of severe illness in the population. To better understand this, let's take a look at several of the countries. Let's first look at Italy. In Italy, the number of cases on Monday was double the number of new cases on November 16, 2020, the peak of Italy's winter surge. Yet the number of patients currently in the ICU on Monday was seven fold lower than the number on November 16th, and the number of deaths were four fold lower. Again, despite there being twice as many cases. Similarly, in France, the number of new cases was double the number of cases on November 7th, 2020 and their winter peak then. But the country saw a nearly three fold lower number of ICU patients and a nearly five fold lower

number of deaths. Cases in Germany on Monday were almost four times higher than they were in their December 23rd, 2020 winter peak. But the country only had about half of the number of ICU patients and just a seventh of the number of deaths. Though some of the reduction in severe disease and death may be due to the lower disease severity with Omicron overall and a better understanding of how to treat COVID, it is likely largely due to vaccines. Keep in mind that during the 2020 winter surge, almost none of the world's population was vaccinated. Today, Italy, France and Germany all have over three fourths of their populations fully vaccinated, with two doses and over half of their populations vaccinated with three doses. And their low numbers of hospitalizations and deaths send a clear message, this vaccine is working. If we compare their numbers to what we're seeing in the US, which has a much lower vaccination rate at 65% fully vaccinated and less than 30% having received a third dose, we see that the reduction in death is much smaller. During the Omicron peak in the US, cases were over three fold higher than they were during the 2020 winter surge peak and deaths are about 1.5 fold lower. This is still a significant reduction in deaths, but it does not compare to what we're currently seeing in Western Europe. So the bottom line is, even though some aspects of the surge in Western Europe remain a bit of a mystery, we are seeing less severe disease and death across the board in the region. Despite the high number of cases, a sign that our vaccines are working and that we are slowly learning to live with this virus. Now let's look over to Eastern Europe at four of the countries we talked about last week that are housing ever increasing numbers of Ukrainian refugees, Poland, Slovakia, Romania and Hungary. Last week I noted the cases in these countries were continuing to decline, but the rates of decrease were slowing. This week, Poland and Slovakia are still seeing case numbers fall, but Romania and Hungary saw an 8% and 73% increase in cases in the last 14 days, respectively. Just as the situation in Western Europe is not entirely clear, we do not know exactly what is causing these upticks in Romania and Hungary, or why Poland and Slovakia have not experienced the same rise in cases. BA.2 recently became dominant in Romania, so it's tempting to assume that the variant must be the cause of this recent rise in cases. But it is far more prevalent in Poland and Slovakia, making up 86 and 93% of the cases respectively. And again, these countries have still not seen an increase in cases. Hungary has not reported any sequencing data since January, so the situation there in regards to BA.2 is unknown. To summarize what I just shared with you again, that really, really important context word, humility. I can't explain to you why what we're seeing happening in Eastern Europe is occurring. It is possible that the strain on the health care systems in these countries caused by the



nearby conflict in Ukraine and the large number of refugees associated with it could be contributing to the rise in cases. But all of these countries have taken in similar numbers of refugees relative to their populations. So, again, this would not explain why some countries are seeing increases, but others not. Finally, just as we saw with Western Europe, the burden of severe disease and death in these countries right now is far lower than previous surges. So even though there are many aspects of the BA.2 surge in Europe that we still understand, it is clear that this surge is not taking as large a toll on the health care system or in terms of deaths as previous surges did.

**Chris Dall:** [00:24:49] That brings us once again to the United States, where the declining cases we've been seeing over the past month seems to have bottomed out and some states are starting to see cases rise again. In addition, BA.2 now accounts for nearly 55% of the circulating coronavirus lineages in the country, according to the CDC. I think a lot of people right now are waiting for the BA.2 wave to begin. Is that what we're going to see here in the next few weeks, or is it possible that we could avoid another wave?

**Michael Osterholm:** [00:25:16] Chris, this is a critical question you're asking and one that I have to be absolutely honest about and say, I don't know, but this is what I do know. The Omicron sub variant BA.2 is now the dominant strain here in the US, accounting for 55% of new cases, up from 35% last week. Despite this, the US overall continues to see a decline in cases now sitting at an overall average of 29,250 cases a day, or about nine per 100,000 individuals. This is 9% lower than the average daily we saw just two weeks ago. The last time we saw case numbers at this level was mid-July 2021, just prior to the Delta surge. Hospitalizations are also the lowest they've been since July 2021, and ICU admissions are the lowest they've been since July 2020. But on Wednesday, COVID-19 hospitalizations were still at nearly 17,500, down 34% from two weeks before and there were 715 daily deaths on average. This is all great news. But now let me share with you reality. While the US overall is seeing decreasing numbers, 13 states and the District of Columbia have seen increasing cases over the past two weeks. Remember that last week only five states were seeing increasing cases? Currently, 11 of the 13 states as well as the District of Columbia, are all seeing double digit increases over two weeks, and five states and the District of Columbia are above 30%. New York has seen a 65% increase compared to a 21% increase last week. However, I want to add context here that the 3,000 cases we're currently seeing

in the state of New York, even with this increase is far, far below the 75,000 cases reported per day back during the Omicron surge. In addition, Connecticut, which was seeing a decrease last week, is now seeing a 64% increase compared to just two weeks ago. Again, their numbers are still relatively low at 378 cases reported per day. Nebraska, Massachusetts and Delaware all above 30% increases. Interestingly, in all the states currently seeing increasing cases are also at the same time seeing double digit decreases in daily hospitalizations. Only Connecticut and Massachusetts are seeing single digit decreases, 8 and 9%, respectively. I believe that these numbers actually represent an inflection point in where we're at. Case numbers are starting to go up, but hospitalizations and deaths still going down could reflect the fact that in 2 to 3 weeks, the hospitalizations and deaths will go up if case numbers continue to rise. We just don't know if that will be the case. As we mentioned the past few weeks, the US has seen an increase in COVID in wastewater across the country. In the past week, New York has identified 150 sites, more than doubling in COVID-19 presents an increase of 25% over a week ago. Another 75 sites have shown increases in activity as well. These wastewater trends mimic the case trends seen in the state. As we've discussed in the past few weeks, congressional funding for pandemic preparedness and response is still up in the air. The administration has explained that several programs will have to be discontinued because of the lack of funding. As of March 22nd, the Health Resources and Services Administration, COVID-19 uninsured program that reimburse providers for the cost of testing and treating the uninsured for COVID stopped accepting claims. They also are set to stop accepting claims for vaccines next week. Without funding, the government will have no way to order more tests, treatments or vaccines once the current supply is depleted. While private purchasers may still have the ability to access these products, a decrease in demand will likely cause manufacturers to shift their attention elsewhere and cause supply chain shortages again. Ultimately, without services like this, we are bound to see the inequitable access to care and the uninsured are going to be hit the hardest. I will discuss the FDA and CDC decision to recommend fourth doses for some Americans later in the podcast. But it is important to just note that the vaccine rates in the US remain low, with only 77% receiving one dose, 65% fully vaccinated or two doses, and only 29% receiving the third dose. And think about how this compares to the other countries I just talked about. We are potentially in for more difficult days ahead. With the decision this past Tuesday, we may see an increase in the number of doses administered in the weeks to come, but these will likely be the same people who have sought out vaccines already. The lack of funding will surely be a

barrier to access and affordability of vaccines, and it may cause some people to make the decision not to seek out a fourth dose. In short, I fear that we will repeat our history, just as we saw with both Delta and Omicron surges. A lack of capacity to respond, for testing, for treating and for surveillance. We are now dismantling all the pieces of what we've put together for Delta and Omicron, because the public and government are basically over this pandemic, despite the fact that this virus is not over us. So all I can say is stay tuned. Hang on. And we're going to have to have lots of humility.

**Chris Dall:** [00:30:52] So, Mike, as you just noted, the FDA on Tuesday authorized a fourth dose of the Pfizer and Moderna vaccines for people ages 15 and older. This was not really unexpected, as it's been hinted at for weeks. But is this the right call by the FDA?

**Michael Osterholm:** [00:31:09] Well, let me just begin by saying that, as with any decision like this, there will be all kinds of armchair quarterbacks who will be determining with great wisdom, but lack of real understanding, the significance of what's happened here. I will try not to be one of those individuals. I'll just give you what I know for the data and where I think we're at. And I'll make it very clear right now, I will always, as a public health professional, basically be proactive versus reactive. And I think what you'll see in a moment is that the US agencies, both the FDA and the CDC, were making every attempt to be proactive. Well, Chris, as you noted, on Tuesday, the FDA authorized a fourth dose, a second booster dose of vaccine for people over the age of 50 and for certain immunocompromised individuals. This was based on data that show waning of protection over time against serious outcomes from COVID-19 in these populations. Data reviewed by the FDA showed that the fourth dose induced high levels of neutralizing antibody, one marker of protection against infection and, more importantly, serious outcomes. Data from a preprint study released this past week conducted in Israel, suggests that the fourth dose adds even more protection against death from COVID. The study looked at over 560,000 participants over the age of 60 who are at least four months out from their initial booster or third dose over a 40 day period from January 10th to February 20th, 2022, meaning the study took place entirely during the Omicron surge. While BA.2 was not dominant during the study period, it was present in the country at the time and almost certainly accounted for some of the cases among study participants in that time period. 58% of the participants received a second booster dose during the study period, while 42% did not. The study found a 78%

reduction in mortality among those who received the second booster compared to those who did not. Though the study only provides information on the short term efficacy of the second booster or fourth dose, it certainly suggests that older populations can benefit from the additional dose. Now, I might add that several of my colleagues who I refer to affectionately as all of us is talking heads were in the media in the past 36 to 48 hours saying there are no data to support the fourth dose approval. Well, I think these are pretty compelling data, even if incomplete. And so I think that argument, unfortunately, is just simply not true. The FDA also reviews safety data for fourth doses and found that the vaccine continues to be safe. A summary of safety surveillance data provided to the FDA by the Ministry of Health of Israel identified no new safety concern after four doses of the Pfizer-Biontech COVID-19 vaccine. It was administered to approximately 700,000 adults at least four months after the third dose. Approximately 600,000 vaccine recipients were 60 years of age and older. CDC followed by updating their recommendations to allow people over the age of 50 and people with certain immunocompromising conditions and who received an initial mRNA booster dose at least four months ago to be eligible for another mRNA booster. As a follow up to our discussion last week, CDC has also updated their guidance for adults who received a primary vaccine and a booster dose of Johnson and Johnson's COVID-19 vaccine at least four months ago. They may now receive a second booster dose using an mRNA COVID-19 vaccine. This is based on data published in the Morbidity Mortality Weekly Report by the CDC on Tuesday that shows that a heterologous or a mix and match dose of mRNA vaccine after a dose of the Johnson and Johnson vaccine is more effective than two Johnson & Johnson doses. The Heterologous combination was 78% effective in preventing hospitalization, compared to 67% for the two doses of Johnson and Johnson and just 31% for a single dose of Johnson and Johnson, but still less effective than three doses of an mRNA vaccine, which was 90% effective in preventing hospitalizations. Even though the new recommendations open the door for some higher risk individuals to better protect themselves, it is unlikely to make an impact on the bigger picture. It has become very clear over the last year that vaccines alone cannot get us out of this pandemic. There are a few key barriers to achieving this. First, not everyone who would like a vaccine has access to a vaccine. 85% of people in low income countries have not yet received a single dose of vaccine until the world has access to vaccines and find a willing population to receive the vaccines and thus vaccinated, boosting our way out of a pandemic cannot even be considered to be a realistic solution to end the pandemic. Second, not everyone who has access to

vaccines is willing to get the vaccine. As I just noted, vaccine hesitancy is going to be another barrier to getting the world vaccinated. Currently, a fourth of the US population has yet to get a single dose of the vaccine, despite it being both free and widely available. Less than half of those who received two doses decided to get a third, which is only 29% of the population. And yet we have time and time again described how important that third dose is with regard to reducing severe illness, hospitalizations and deaths. While it looks like these additional booster doses will reduce disease severity and death, especially in high risk populations, it is not a sustainable or practical long term solution. We do need vaccines that are more durable and broadly protective. We certainly will not be able to boost our way out of this pandemic, especially when much of the world has yet to receive even a first dose. At this point, we must use the tools we have, but we must also work diligently to find even better tools, i.e. generation two, generation three, and generation four COVID-19 vaccines.

**Chris Dall:** [00:37:34] So Mike, I don't insert myself into this podcast very often, but I'm going to here because maybe I can serve as a bit of a proxy for members of our audience. I am 50 years old. I am just about four months out from my third dose of the Pfizer vaccine. I'm a healthy individual. I have no comorbidities, but I am looking to get out more in the world. Over the next few months, I'll be returning to the office. Should I get a booster dose?

**Michael Osterholm:** [00:38:01] Well, Chris, that's a question we're all asking ourselves, because I'm an older individual I already fall into that category of getting the vaccine. But I appreciate very much where you're coming from. But let's be very clear. There are two buckets of concern about receiving a COVID-19 vaccine. One is, how well does it protect? What does it do? Does it make a difference? And number two is, is it safe? Is there a cost to getting that vaccine that I need to weigh against the benefit? Let me just dispel that second bucket first. As you just heard my answer with regard to the Israeli data, looking at potential adverse events associated with the vaccine. Yes, there have been very rare events relative to the millions of people who have been vaccinated, but these are very, very low event situations. So from my perspective, I look, then what's the benefit? And I think the Israeli data as it goes down as far as 60 years, not 50 years. I do believe there is a benefit. As you know, on this podcast dating way back to last summer, I very strongly supported third dose vaccinations as what I thought should be part of the Prime Series, and I did that based on what I would consider incomplete

information. But in public health, we don't always have the luxury of waiting until you have the definitive answer to protect people's lives. Every day you don't act, could mean more people could be harmed because of your inaction. Well, that was greatly debated as to how beneficial these third doses would be, particularly, again, by some of the talking heads. Well, within the last 6 to 8 weeks, we have come up with compelling data, compelling data that third doses all the way down to teen years reduce significantly, reduce the incidence of severe illness, hospitalizations and deaths, not just in those over 65, not just those over 50, not just those over 30, all the way down to the younger individuals. And so I believe that the fourth dose ultimately will do some of those same things. And why would you not want to get that benefit right now? So I don't know how long that protection will last. I think we're all in a world right now of trying to understand what our future looks like with the current generation one vaccines we have. But that should not be a deterrence to using them, even if it's not going to stop you from becoming infected. But it can have a tremendous impact on whether you are hospitalized, seriously ill or not, and particularly for those, again, who are immune compromised, I cannot state it any more clearly. This is your lifeline. It's the best one you have. Please get vaccinated now with the four doses, get your shot. And I would urge you to get your shot because we need you so badly as CIDRAP every day that if you're not there, we will miss you immensely. We will also miss you personally. So get your shot.

**Chris Dall:** [00:41:11] On another FDA note, the FDA last week stopped the further deployment of the monoclonal antibody sotrovimab in certain places of the country where BA.2 variant is now causing the majority of infections. This takes one treatment off the shelf as the country faces a possible surge in infections. Mike, given the emphasis the administration is putting on the test and treat strategy, is this a concern?

**Michael Osterholm:** [00:41:38] Chris, any time we lose a critical tool in reducing the burden of severe illness, it's a challenge, particularly with this disease. Let me just summarize the situation. Sotrovimab had maintained its efficacy against Omicron BA.1. Unlike several others like the Lilly and Regeneron products. As you know, the US stopped distributing these when Omicron became dominant. However, recent lab studies now have shown that Sotrovimab is also not effective in neutralizing the BA.2 lineage. Due to the loss of efficacy in the lab, the FDA is scaling back the distribution of the treatment and has stopped any further deployment of the drug to areas where BA.2

is dominant. I believe that this will occur virtually everywhere in the country shortly as we're seeing the rapid rise of BA.2 in each of our communities. The number of Sotrovimab courses ordered had already decreased during the past few weeks, but it has not yet been paused completely. The HHS distribution tracker shows that there are only currently five different therapies in the US monoclonal arsenal, with Sotrovimab being one of them. Last week, 335,000 total courses of monoclonal antibody therapy were distributed and just under 30,000 of those being sotrovimab. We'll have to wait and see what happens with cases, but I think we could surely be challenged to have adequate monoclonal antibody treatments in the future should we see this surge here in the United States that's been seen in Europe. Fortunately, we still do have a few other options available that appear to be effective at neutralizing BA.2. The FDA approved the Eli Lilly monoclonal antibody treatment about a month ago. That is designed specifically for the BA.2 lineage. The US government ordered 600,000 courses of this treatment last month and just over half of those has been distributed so far, with 30,000 being distributed just last week. Again, the challenge is going to be the US government's ability to buy this drug and distribute it. It's unclear right now how the private sector might pick it up. Can they pick it up? What will be the shortage for drug needed versus drug available? And I think these are all really critical questions. This is a really unfortunate situation. But both the viruses presented in terms of the changes with the mutations and the effectiveness of the drug, but also it's about our own country's ability to finance the health care that could save so many lives. Every person who gets an effective monoclonal antibody treatment is just one less person we have to worry about long term hospitalization, serious illness and even death.

**Chris Dall:** [00:44:23] That brings us to this week's COVID query, which deals with how Africa has fared during the pandemic. Bob wrote "Early in the pandemic, I feared that Africa would be crushed by the virus because of a combination of relatively more crowded households and a less robust health care system than we enjoy in the West. But the horror stories I expected from that continent have mostly not come. So I'm curious, is this a matter of inadequate public health surveillance on the ground, lack of media attention? Or has it really been not a big problem there? And if that's true, then do we know anything about why such an obvious target has been relatively spared?" And Mike, this is a great question that I think a lot of experts are asking as well. What is going on in Africa?

**Michael Osterholm:** [00:45:06] Well, first of all, I want to thank Bob for asking this very thoughtful question, and one that is a question for many of us who work every day in the COVID-19 world. When looking at the data on a surface level, it appears that Africa has done exceptionally well with COVID. Many countries in sub-Saharan Africa have some of the lowest cumulative COVID cases and deaths reported per 100,000 population in the world. But when we consider that most countries in Africa lack the ability to test and report cases, the numbers actually, I think, tell a very different story. As of Monday, South Africa has done a total of 396 COVID tests per 1,000 population throughout the entire pandemic, Zambia has done 176, Zimbabwe 144, Sierra Leone 48, Nigeria 22. And many countries like Tanzania, Liberia and the Democratic Republic of the Congo have not reported any data on the number of tests completed at all. For reference, the United States has done over 2,500 COVID tests per 1,000 population, the UK over 7,000 and Denmark over 11,000. Again, some European countries have done over 10,000 tests per 1,000 population. That's over ten tests per person, compared to some other African countries that have done less than two tests per 100 people. So with so little testing being reported from many countries in sub-Saharan Africa, the question is not about is there more transmission occurring in this region than the numbers would suggest, but how much more transmission and how many more deaths? A few studies have been done to attempt to answer these questions. One study, published in the Emerging Infectious Diseases Journal in September, looked at the seroprevalence data from randomly selected cohorts from two communities in South Africa, one rural and one urban. The seroprevalence was 7% and 26% after the first wave and 26 and 41% after the second wave in the rural and urban cohorts, respectively. The study estimated that 95% of the infections in these communities were not nationally reported. This means only 5% of these cases were nationally reported. And remember, this is South Africa, which has reported more testing than most other sub-Saharan African countries. A preprint study released this past week found that one third of over 1,100 bodies tested from a morgue in Zambia in 2020 and 2021 were found to be positive for COVID. Let me just repeat that. One third of over 1,100 bodies tested were positive for COVID during the beta and delta peaks, this was as high as 90%. Out of the 358 bodies that tested positive, only 10% had tested positive while still alive. Some of the other 90% had false negative tests, but mostly were simply never tested prior to death. Just as there has been concern about this vast underreporting of cases, it's also unclear the extent to which serious cases and deaths have gone underreported in the region. The Zambia study looked at the cause of death for all the adult patients that tested positive



for COVID after death and found that over 70% died possibly or probably due to COVID. The other 30% were either deemed as having probably not died of COVID, or there was insufficient evidence to determine the cause. Many countries in this region do not report national mortality data, which makes it difficult to know the extent of excess deaths among COVID-19 patients. There's been some speculation that Africa's young population may be somewhat protected from COVID simply due to their age. But at least in this study, that did not appear to be the case. Over 25% of the people in all age groups in the study tested positive, and the weighted median age of death was 48 years, indicating that young people in the study were certainly still at risk of dying from COVID. There are a number of factors that put Africa's population at risk despite the average young age, the first being poor access to health care. In the study of Zambia, four out of five people that tested positive after death were never hospitalized. Therefore, it's not possible to say that the lack of increased hospitalization means that there was no evidence of COVID in the community. Though we know in this study in Zambia it's possible that not all of them died from COVID, we know that many of them likely did. And it is possible that had they been able to be admitted to hospital, they may have survived. The second factor that may be contributing to COVID deaths in sub-Saharan Africa is the lack of access to vaccination. If we look at some of the countries you discussed earlier in regards to low testing capacity, all have very low vaccination rates with South Africa 30%, Zambia 12%, Zimbabwe at 24%, Sierra Leone at 14%, Nigeria at 5% and the Democratic Republic of the Congo at less than 1%. Only a small, small percentage of people in the region have received a third dose. This lack of protection from vaccination means that despite the young population, there could be a significant amount of COVID deaths occurring in the region. And a third factor that may be contributing to COVID deaths is the large percentage of populations in these countries that are increased risk of developing severe illness from COVID due to HIV/AIDS. The prevalence of HIV/AIDS in adults is over 10% in eight countries in sub-Saharan Africa, including South Africa, Zambia and Zimbabwe. This high prevalence of HIV infection, especially given the barriers many people in these countries face in accessing HIV treatment, puts a significant amount of their populations at increased risk of dying from COVID. We still have very little information on just how many COVID deaths that this region has experienced. But these factors poor access to medical care, low vaccination rates, and HIV/AIDS prevalence, along with the evidence of vast underreporting of cases, gives us a strong reason to believe that this region has experienced a significant amount of severe COVID and COVID death. Unfortunately, we

may never know the extent of it, though, as more studies similar to the ones we referenced earlier are published hopefully there will be more clarity as to what really happened and what is continuing to happen in this region.

**Chris Dall:** [00:51:46] Mike, what can you tell us about our latest beautiful place submission?

**Michael Osterholm:** [00:51:52] Chris, again, we have another one of those, what I would call beautiful places geographically and beautiful places in the mind. This is from Margi in Bellingham, Washington. And she wrote, "Thank you for your weekly podcast. I've listened to every Thursday since I first discovered CIDRAP last August. I especially appreciate your willingness to discuss the many uncertainties of this pandemic. I know we don't have clear answers or an ability to predict the future, but I'm grateful for your guidance and its clear thinking. I'm also thankful for the weekly reminders of the importance of kindness made even more poignant when Dr. Osterholm shared his early experience over the holidays. Attached are pictures of my beautiful place, aptly named for these times "Burnout." Every Sunday during the pandemic, my husband and I have hiked up the burnout road not far from our home in northwest Washington. The dirt road is closed to motorized vehicles and is open to hikers and bicyclists. Sometimes we go up and back and sometimes we loop around through the Larrabee State Park and the Lost Lake Trail. Often I go alone on this nine mile hike during the week. The views of the sky, water, islands and mountains are ever changing and spectacular. On a clear day, you can see Mount Baker, Mount Rainier and the Olympic Mountains. These vistas come at a cost. The area has been logged off the names, burnout and lost and the walk through the clear cuts are fitting symbols for the time we live in. And yet the beauty transcends. I will always be grateful for the gift of open sky for the time with my spouse, for the people I've met there who've told me their stories, or simply smiled as we passed. Through it all the grief and the anxiety of these past two years, I found solace by being outdoors and moving through the imperfect world. Solvitur ambulando, it is solved by walking. I hope your listeners will also find a little solace in these photos. Thank you again, Margi." Thank you so much for this very thoughtful, beautiful place. The pictures are stunning. Please I hope everyone listening takes a moment to go to the website and look at these pictures that have been shared. It is a beautiful place. This is the beauty in the world we must never, ever, ever forget.

**Chris Dall:** [00:54:11] And as we wrap up here, Mike, what are your take home messages for today?

**Michael Osterholm:** [00:54:16] Well, Chris, I've got three messages that I think resonate throughout this podcast. One is BA.2 and the unknown. We just don't know what this virus is going to do here in the United States. We see what it's doing in Europe. We know what it's doing in Asia. It's unclear what it's doing in the rest of the world, the Americas, for example. What is it doing in Africa? We're not sure. This, again, is going to be one of those wait and watch with one exception. We know that vaccinations can have a tremendous impact on the incidence of severe illness, hospitalizations and deaths. And that leads me to my second point. I will repeat it again probably every podcast from now until infinity. Vaccines, vaccines, vaccines. They're not perfect. Far from it. But they're remarkable tools. I can't emphasize how important this can be to preventing a very, very tragic moment in your life. And finally, the third point is something I learned kind of as a young kid in Iowa, and that is you don't take your Christmas tree down on December 10th. It's supposed to stay up for another couple of weeks. And I feel like that's what we're doing right now with the public health infrastructure to respond to COVID. We are watching it be dismantled. Testing sites are shutting down. We're seeing disease surveillance activities in many states curtailed. We're seeing a real challenge in getting adequate drugs and monoclonal antibodies to treatment sites. I understand that many Americans are done with this pandemic, but as I say, time and time again, the virus is not done with us. Our US government can't at this moment be absent without leave. We've been here before. We got burned with Delta. We got burned with Omicron. How many times do we have to learn that if we don't have infrastructure in place, when a potential surge occurs, we will pay a price. To me, this is a simple lesson. You know, you don't order your fire trucks at the moment a 911 call comes in and you don't sell them to somebody else when you get back to the station. I realize this is a cost. I realize that this is not necessarily cheap to keep infrastructure in place, but if you don't have it when a surge occurs, you're in trouble. And I think the right now, as I just said in point one, I don't know what BA.2 is going to do, but it could be a real challenge in the weeks ahead. So please, Congress fund these programs. I will promise you there is no fat in any of them. I will promise you that the money will be spent for the very things we just talked about, which is going to save lives. So to me, that is such an important message, and I hope all of you get that to your elected officials.

**Chris Dall:** [00:57:11] And your closing song for today.

**Michael Osterholm:** [00:57:15] Well, let me begin by saying, first of all, thank you again for being with us. I just want to pick up where I started this podcast with the gratitude that we have for you as listeners and all you do to help our world as much as we could ever help your world. I noted in the opening about an email that I had received from Virginia in Houston that was so touching to me. And what was notable about it is it came shortly after I had received a very, very vile, angry, threatening letter. And I can tell you that they both impact me, but there was no doubt about it, kindness trumped the pain completely. And you have done that so many times for us. I hope that we can do some of that for you. And it's in that light that I picked our closing today to share with you, because I think it follows on the theme that we're talking about. This is a song that we've used before, an Episode 54 on May 6th of 2021. The title was "Vaccines and Taking Care of Friends." This is "Friends," a song written by English musician Elton John and songwriter Bernie Taupin and performed by Elton John. As you know, it was John's third US hit and his second to reach the top 40 after his breakthrough success of "Your Song," Ironically, "Friends" was not the follow up to the single "Your Song," but was rather the title track and theme song for the movie "Friends" starring Sean Bury. And it was included in the soundtrack. It was the only hit from that LP. The song rose to number 34 on the US Billboard Hot 100 and number 17 on the Cashbox, Top 100. On the Canadian Singles chart, "Friends" peaked at number 13. "Friends" also became a hit on the adult contemporary charts of both nations. The song, which was actually released on March 10th, 1971, my birthday, had been recorded in September 1970. Here it is song written by Bernie Taupin and sung by Elton John, "Friends." "I hope the day will be a lighter highway for friends that are found in every road. Can you think of any better way for the lost and weary travelers to go? Making friends for the world to see, let the people know you got what you need. With a friend at hand, you will see the light. If your friends are there, then everything's all right. It seems to me a crime that we should age. These fragile times should never slip us by. A time you never can or shall erase. As friends together, watch their childhood fly. Making friends for the world to see. Let the people know you got what you need. With a friend at hand, you will see the light. If your friends are there, then everything's all right. Making friends for the world to see. Let the people know you got what you need. With a friend at hand, you will see the light. If your friends are there, then everything's all right." Elton John. Bernie Taupin. Thank

you, friends, for being with us again for another week. We appreciate it. I just remind us all as we close on this podcast with these decrease in numbers that we still have suffered a great deal of pain over the past two years. We've lost a lot of loved ones family, friends, colleagues, and we must never forget what all that means. Thank you again for being part of this podcast. Everyone be kind. Be safe this week. Be prepared for what may be coming, but enjoy life right now as much as you possibly can. Be kind. Be safe. Thank you for being with us.

**Chris Dall:** [01:01:09] Thanks for listening to this week's episode of the Osterholm update. If you're enjoying the podcast, please subscribe, rate, and review, and be sure to keep up with the latest COVID-19 news by visiting our website [CIDRAP.umn.edu](http://CIDRAP.umn.edu). This podcast is supported in part by you, our listeners. If you would like to donate, please go to [CIDRAP.umn.edu/donate-now](http://CIDRAP.umn.edu/donate-now). The Osterholm update is produced by Maya Peters, Cory Anderson, Angela Ulrich, Meredith Arpey, and Sydney Redepenning.